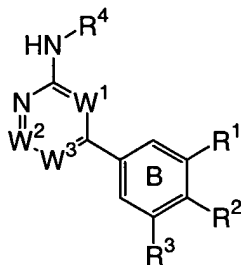


CLAIMS

1. A compound of formula I:



I

or a pharmaceutically acceptable salt thereof, wherein:

W¹ is nitrogen or CH, W² is nitrogen or C-(U)_pR^U, and W³ is nitrogen or C-(V)_qR^V;

p and q are each independently 0 or 1;

R^U and R^V are each independently R or Ar¹;

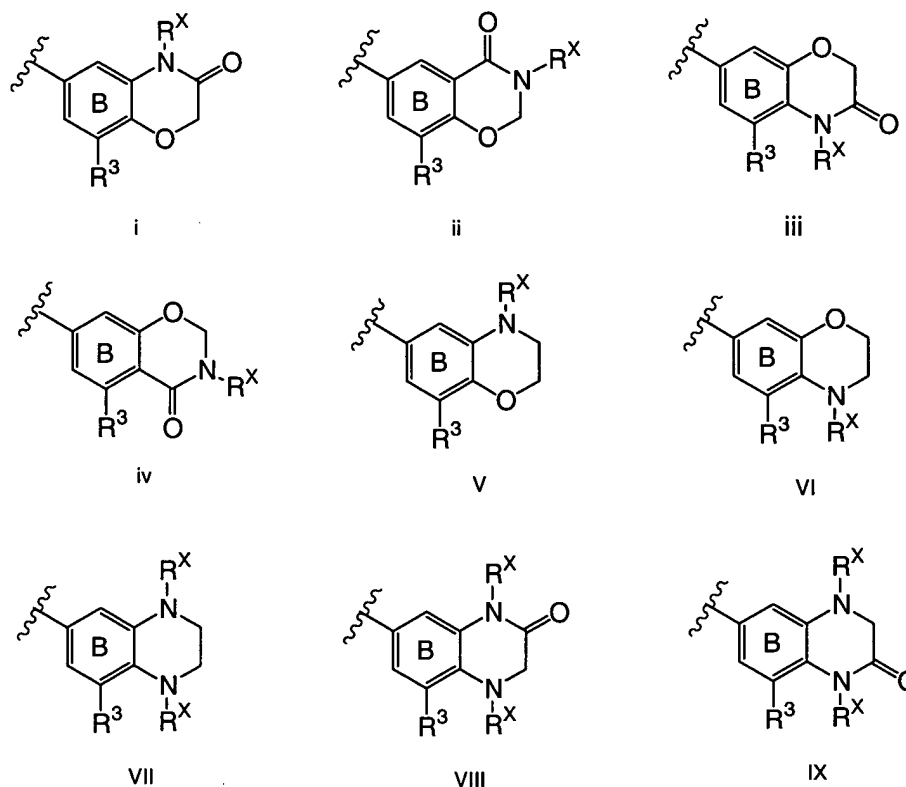
U and V are each independently a bond or a C₁₋₆ alkylidene chain, wherein up to two methylene units of the chain are optionally and independently replaced by CO, CO₂, COCO, CONR, OCONR, NRNR, NRNRCO, NRCO, NRCO₂, NRCONR, SO, SO₂, NRSO₂, SO₂NR, NRSO₂NR, O, S, or NR;

each occurrence of R is independently hydrogen or an optionally substituted C₁₋₄ aliphatic, or two R bound to the same nitrogen atom are optionally taken together with the nitrogen atom to form a 3-7 membered saturated, partially unsaturated, or fully unsaturated ring having 0-2 additional heteroatoms independently selected from nitrogen, oxygen, or sulfur;

Ar¹ is a 5-7 membered saturated, partially unsaturated, or fully unsaturated monocyclic ring having 0-3 heteroatoms independently selected from nitrogen, oxygen, or sulfur, or an 8-12 membered saturated, partially unsaturated, or fully unsaturated bicyclic ring system having 0-5 heteroatoms independently selected from nitrogen, oxygen, or sulfur; wherein Ar¹ is optionally substituted with m independent occurrences of Z-R⁵; wherein m is 0-5, Z is a bond or is a C₁₋₆ alkylidene chain wherein up to two methylene units of Z are optionally replaced by CO, CO₂, COCO, CONR, OCONR, NRNR, NRNRCO, NRCO,

NRCO₂, NRCONR, SO, SO₂, NRSO₂, SO₂NR, NRSO₂NR, O, S, or NR; and each occurrence of R⁵ is independently hydrogen, an optionally substituted aliphatic, heteroaliphatic, aryl or heteroaryl group, halogen, NO₂, CN, OR, SR, N(R)₂, NRCOR, NRCON(R)₂, NRCO₂R, COR, CO₂R, OCOR, CON(R)₂, OCON(R)₂, SOR, SO₂R, SO₂N(R)₂, NRSO₂R, NRSO₂N(R)₂, COCOR, or COCH₂COR;

R¹ and R² taken together and fused to ring B form a cyclic moiety selected from one of the following:



wherein each occurrence of R^x is independently hydrogen, QR, or Q_nAr¹; n is zero or one; and Q is an optionally substituted C₁₋₄ alkylidene chain wherein one methylene unit of Q is optionally replaced by CO, CO₂, COCO, CONR, OCONR, NRNR, NRNRCO, NRCO, NRCO₂, NRCONR, SO, SO₂, NRSO₂, SO₂NR, NRSO₂NR, O, S, or NR;

R³ is halogen, QR, Q_nCN, Q_nNO₂, or Q_nAr¹; and

R⁴ is Ar¹, or T-Ar¹;

wherein T is a C₁₋₂ alkylidene chain wherein one methylene unit of T is optionally replaced by CO, CO₂, COCO, CONR, OCONR, NRNR, NRNRCO, NRCO, NRCO₂, NRCONR, SO, SO₂, NRSO₂, SO₂NR, NRSO₂NR, O, S, or NR.

2. The compound of claim 1, wherein R¹ and R² taken together represent heterocycle i and R^x is hydrogen or optionally substituted C₁₋₆aliphatic.

3. The compound of claim 1, wherein R^x is hydrogen, methyl, ethyl, propyl, n-butyl, tert-butyl, pentyl, cyclopentyl, hexyl, cyclohexyl, C₁₋₆alkyl substituted with N(R)₂, or C₁₋₆alkyl substituted with Ar¹.

4. The compound of claim 1, wherein R^x is hydrogen, methyl, or C₁₋₂alkyl substituted with a group selected from optionally substituted phenyl, pyridyl, morpholino, piperidinyl, or piperazinyl.

5. The compound of claim 1, wherein R³ is hydrogen, halogen, QR or QAr¹, wherein Q is a C₁₋₃ alkylidene chain wherein one methylene unit of Q is optionally replaced by -O-, -S-, -NHCO-, or -NR-, and Ar¹ is an optionally substituted 5-6 membered saturated, partially unsaturated, or fully unsaturated ring having 0-2 heteroatoms independently selected from nitrogen, oxygen, or sulfur.

6. The compound of claim 1, wherein R³ is hydrogen, OH, OCH₃, OCH₂CH₃, NHCOMe, NH₂, NH(C₁₋₄ aliphatic), N(C₁₋₄ aliphatic)₂, O(CH₂)₂morpholin-4-yl, O(CH₂)₂NH₂, O(CH₂)₂NH(C₁₋₄ aliphatic), O(CH₂)₂N(C₁₋₄ aliphatic)₂, Br, Cl, or F.

7. The compound of claim 1, wherein R³ is hydrogen.

8. The compound of claim 1, wherein R⁴ is a 6-membered saturated, partially unsaturated, or aryl ring having 0-3 nitrogens, a 9-10 membered bicyclic aryl ring having 0-2 nitrogen atoms,

or a 5 membered heteroaryl ring having 2-3 heteroatoms independently selected from nitrogen, oxygen, or sulfur, wherein each ring is optionally substituted.

9. The compound of claim 1, wherein R^4 is optionally substituted phenyl, cyclohexyl, naphthyl, pyridyl, pyrimidinyl, triazinyl, thiazolyl, thiadiazolyl, pyrazolyl, isoxazolyl, indazolyl, or benzimidazolyl.

10. The compound of claim 1, wherein R^4 is an optionally substituted phenyl group.

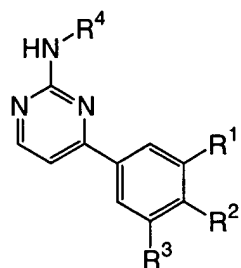
11. The compound of claim 8, wherein each occurrence of Z is independently a bond or a C_{1-4} alkylidene chain wherein one methylene unit of Z is optionally replaced by -O-, -S-, -SO₂-, or -NH-; and each occurrence of R^5 is independently hydrogen, C_{1-6} aliphatic, halogen, NO₂, OR, N(R)₂, or optionally substituted phenyl, pyridyl, or pyrimidinyl.

12. The compound of claim 8, wherein each occurrence of ZR^5 is independently Cl, F, Br, methyl, ethyl, t-butyl, isopropyl, cyclopropyl, nitro, CN, OMe, OEt, CF₃, NH₂, phenyl, benzyl, benzyloxy, OH, methylene dioxy, SO₂NH₂, CONH₂, CO₂Me, phenoxy, O-pyridinyl, SO₂phenyl, nitrophenoxy, aminophenoxy, S-dimethylpyrimidine, NHphenyl, NH-methoxyphenyl, pyridinyl, aminophenyl, phenol, chloro-fluoro-phenyl, dimethylaminophenyl, CF₃-phenyl, dimethylphenyl, chlorophenyl, fluorophenyl, methoxyphenoxy, chlorophenoxy, ethoxyphenoxy, and fluorophenoxy.

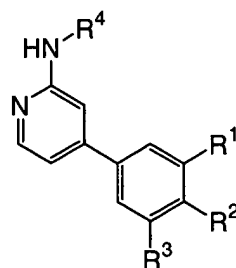
13. The compound of claim 1, wherein $(U)_pR^U$ and $(V)_qR^V$ are each independently hydrogen, halogen, NO₂, CN, OR, SR or N(R)₂, or C_{1-4} aliphatic optionally substituted with oxo, OR, SR, N(R)₂, halogen, NO₂ or CN.

14. The compound of claim 1, wherein $(U)_pR^U$ and $(V)_qR^V$ are each independently hydrogen, Me, OH, or OMe.

15. The compound of claim 1, wherein W^1 is N or CH and compounds have the structure of Formula **Ia** or **Ib**:



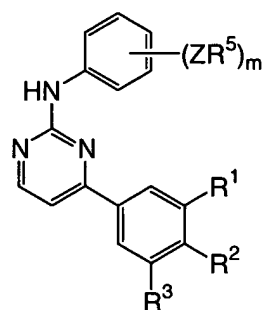
Ia



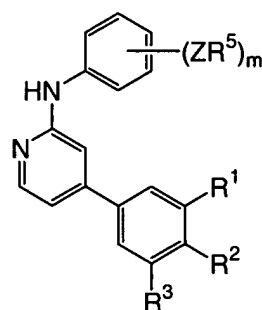
Ib

or a pharmaceutically acceptable salt thereof.

16. The compound of claim 1, wherein R^4 is an optionally substituted phenyl group and compounds have the structure of Formula **IIa** or **IIb**:



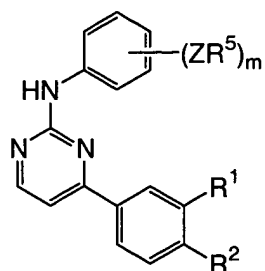
IIa



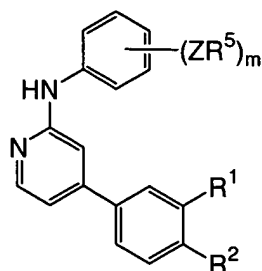
IIb

or a pharmaceutically acceptable salt thereof.

17. The compound of claim 1, wherein R^3 is hydrogen, and compounds have the general structure of Formula **IIIa** or **IIIb**:



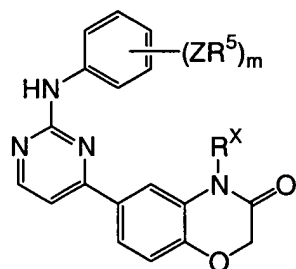
IIIa



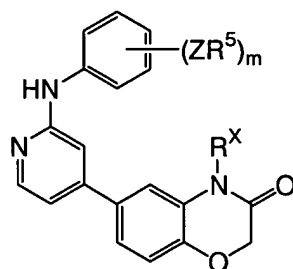
IIIb

or a pharmaceutically acceptable salt thereof.

18. The compound of claim 1, wherein R^3 is hydrogen, and R^1 and R^2 taken together represent the heterocycle **i** and compounds have the general structure of Formula **IVa** or **IVb**:



IVa



IVb

or a pharmaceutically acceptable salt thereof.

19. The compound of any one of claims 15, 16, 17 or 18, wherein

i) R^1 and R^2 taken together represent the heterocycle **i** depicted above; where R^X is defined according to one of the following groups:

- hydrogen or optionally substituted C_{1-6} aliphatic;
- hydrogen, methyl, ethyl, propyl, n-butyl, tert-butyl, pentyl, cyclopentyl, hexyl, cyclohexyl, C_{1-6} alkyl substituted with $N(R)_2$, or C_{1-6} alkyl substituted with Ar^1 ; or
- hydrogen, methyl, or C_{1-2} alkyl substituted with a group selected from optionally substituted phenyl, pyridyl, morpholino, piperidinyl, or piperazinyl.

ii) R^3 is defined according to one of the following groups:

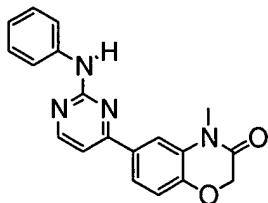
- a. hydrogen, halogen, QR or QAr¹, wherein Q is a C₁₋₃ alkylidene chain wherein one methylene unit of Q is optionally replaced by -O-, -S-, -NHCO-, or -NR-, and Ar¹ is an optionally substituted 5-6 membered saturated, partially unsaturated, or fully unsaturated ring having 0-2 heteroatoms independently selected from nitrogen, oxygen, or sulfur;
 - b. hydrogen, OH, OCH₃, OCH₂CH₃, NHCOMe, NH₂, NH(C₁₋₄ aliphatic), N(C₁₋₄ aliphatic)₂, O(CH₂)₂morpholin-4-yl, O(CH₂)₂NH₂, O(CH₂)₂NH(C₁₋₄ aliphatic), O(CH₂)₂N(C₁₋₄ aliphatic)₂, bromo, chloro, or fluoro; or
 - c. hydrogen;
- iii) R⁴ is defined according to one of the following groups:
- a. a 6-membered saturated, partially unsaturated, or aryl ring having 0-3 nitrogens, a 9-10 membered bicyclic aryl ring having 0-2 nitrogens, or a 5 membered heteroaryl ring having 2-3 heteroatoms independently selected from nitrogen, oxygen, or sulfur, wherein each ring is optionally substituted;
 - b. an optionally substituted ring selected from phenyl, cyclohexyl, naphthyl, pyridyl, pyrimidinyl, triazinyl, thiazolyl, thiadiazolyl, pyrazolyl, isoxazolyl, indazolyl, or benzimidazolyl; or
 - c. an optionally substituted phenyl group;
- iv) W¹, W² and W³ are defined according to one of the following groups:
- a. W¹ is nitrogen or CH, W² is nitrogen or C-(U)_pR^U, and W³ is nitrogen or C-(V)_qR^V;
 - b. W¹ is nitrogen or CH, W² is C-(U)_pR^U, and W³ is C-(V)_qR^V; or
 - c. W¹ is nitrogen or CH and W² and W³ are each CH; and
- v) (U)_pR^U and (V)_qR^V groups are defined according to one of the following groups:
- a. hydrogen, halogen, NO₂, CN, OR, SR or N(R)₂, or C₁₋₄aliphatic optionally substituted with oxo, OR, SR, N(R)₂, halogen, NO₂ or CN;
 - b. hydrogen, Me, OH, OMe or N(R)₂; or
 - c. both (U)_pR^U and (V)_qR^V are hydrogen.

20. The compound of claim 19, wherein each occurrence of Z is independently a bond or a C₁₋₄ alkylidene chain wherein one methylene unit of Z is optionally replaced by -O-, -S-, -SO₂-, or -NH-; and each occurrence of R⁵ is independently hydrogen, C₁₋₆ aliphatic, halogen, NO₂, OR, N(R)₂, or optionally substituted phenyl, pyridyl, and pyrimidinyl.

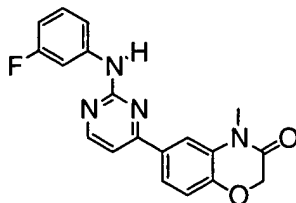
21. The compound of claim 19, wherein each occurrence of ZR⁵ is independently Cl, F, Br, methyl, ethyl, t-butyl, isopropyl, cyclopropyl, nitro, CN, OMe, OEt, CF₃, NH₂, phenyl, benzyl, benzyloxy, OH, methylene dioxy, SO₂NH₂, CONH₂, CO₂Me, phenoxy, O-pyridinyl, SO₂phenyl, nitrophenoxy, aminophenoxy, S-dimethylpyrimidine, NHphenyl, NH-methoxyphenyl, pyridinyl, aminophenyl, phenol, chloro-fluoro-phenyl, dimethylaminophenyl, CF₃-phenyl, dimethylphenyl, chlorophenyl, fluorophenyl, methoxyphenoxy, chlorophenoxy, ethoxyphenoxy, or fluorophenoxy.

22. The compound of claim 1, having the formula **IVa**, wherein R^x is hydrogen or optionally substituted C₁₋₆aliphatic; m is 0, 1 or 2; and ZR⁵ is Cl, F, Br, methyl, ethyl, t-butyl, isopropyl, cyclopropyl, nitro, CN, OMe, OEt, CF₃, NH₂, phenyl, benzyl, benzyloxy, OH, methylene dioxy, SO₂NH₂, CONH₂, CO₂Me, phenoxy, O-pyridinyl, SO₂phenyl, nitrophenoxy, aminophenoxy, S-dimethylpyrimidine, NHphenyl, NH-methoxyphenyl, pyridinyl, aminophenyl, phenol, chloro-fluoro-phenyl, dimethylaminophenyl, CF₃-phenyl, dimethylphenyl, chlorophenyl, fluorophenyl, methoxyphenoxy, chlorophenoxy, ethoxyphenoxy, or fluorophenoxy.

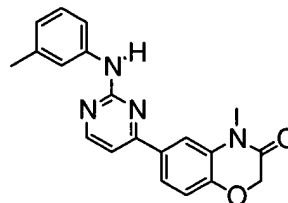
23. The compound of claim 1, selected from one of the following compounds:



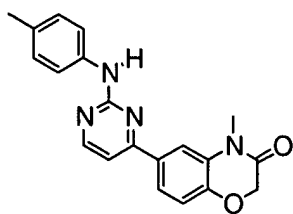
IVa-1



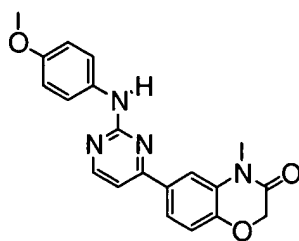
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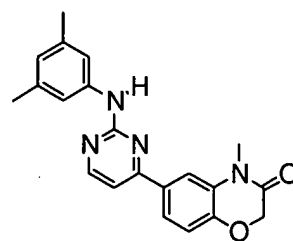
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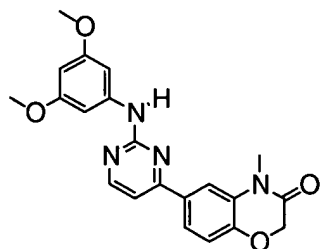
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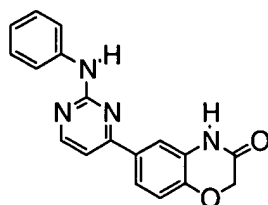
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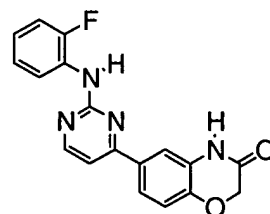
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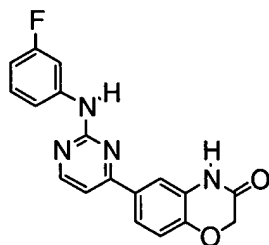
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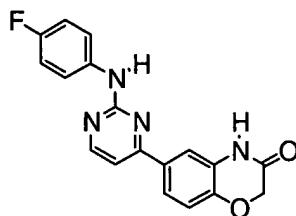
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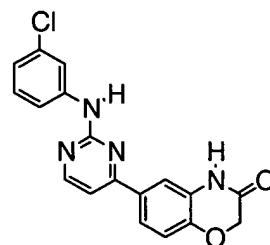
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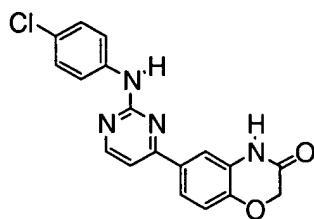
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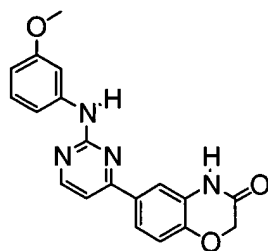
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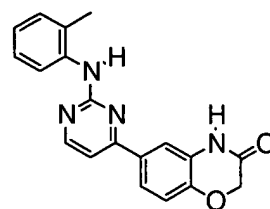
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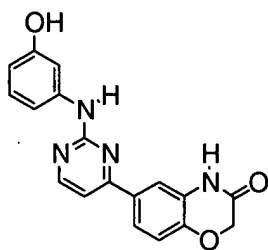
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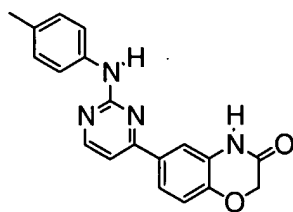
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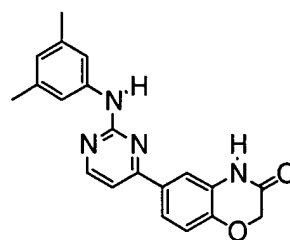
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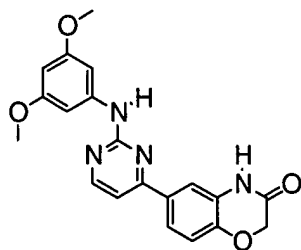
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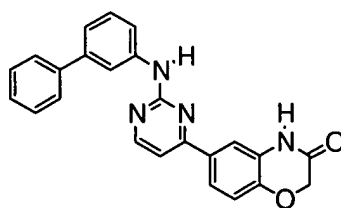
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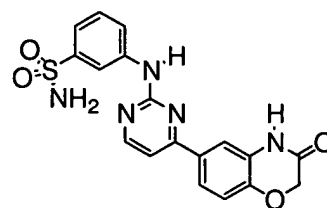
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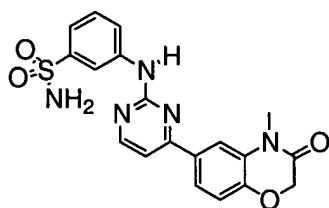
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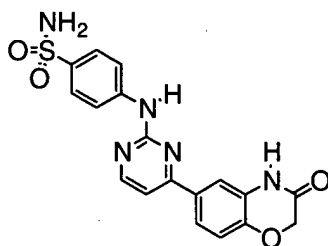
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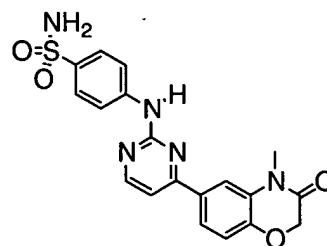
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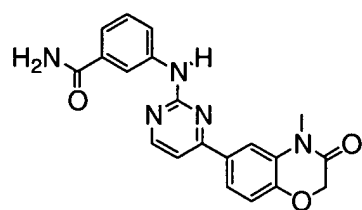
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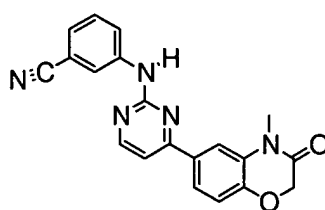
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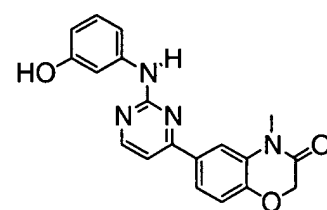
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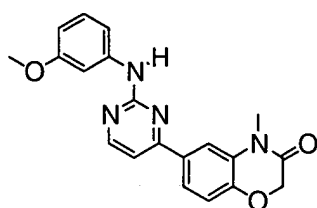
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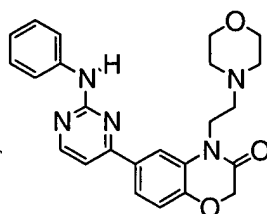
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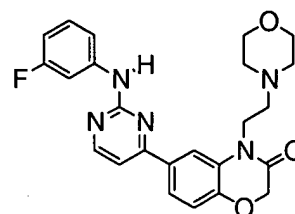
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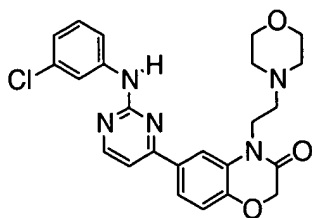
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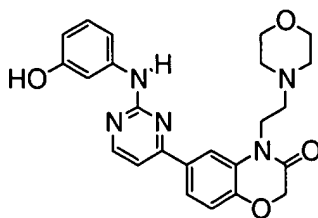
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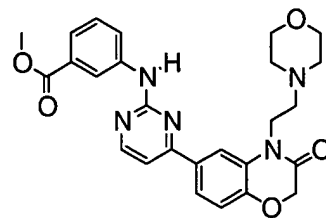
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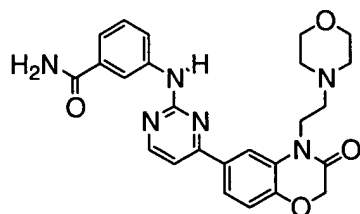
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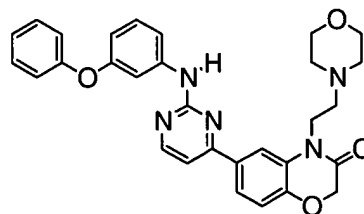
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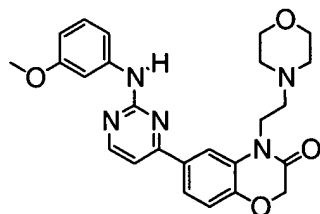
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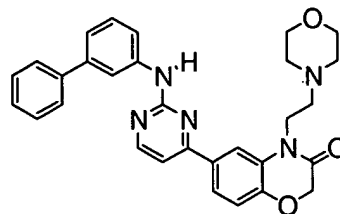
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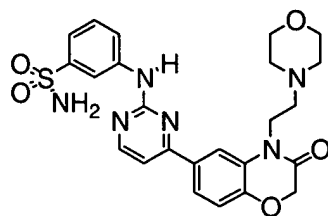
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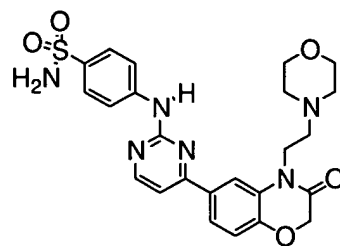
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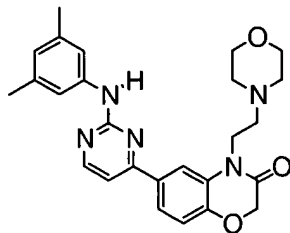
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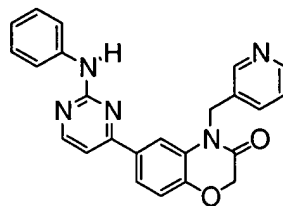
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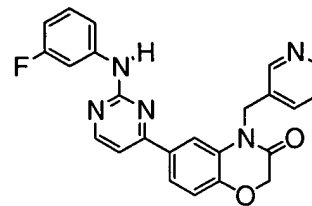
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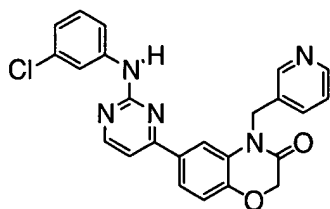
IVa-40



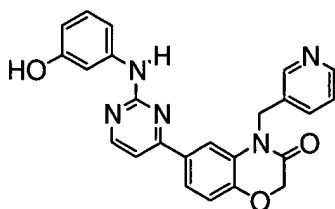
IVa-41



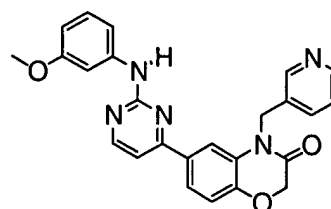
IVa-42



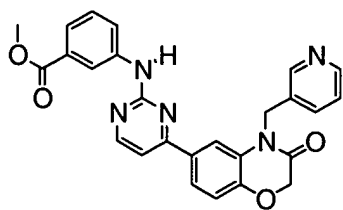
IVa-43



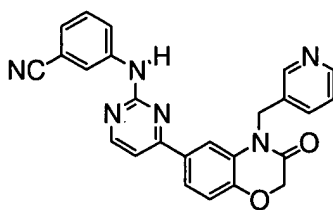
IVa-44



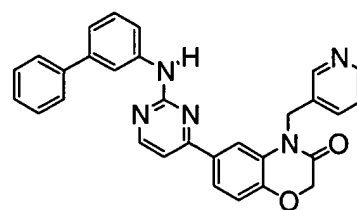
IVa-45



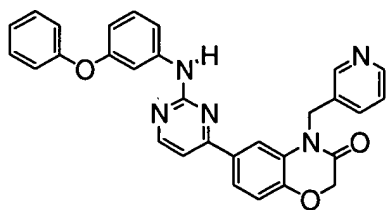
IVa-46



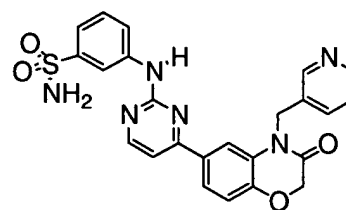
IVa-47



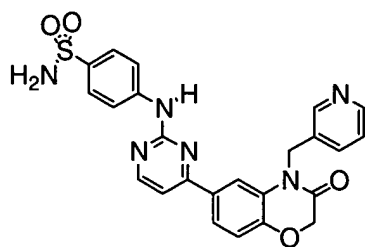
IVa-48



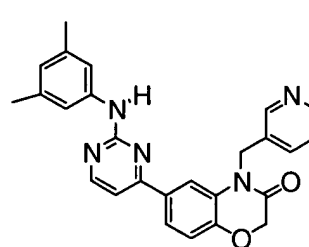
IVa-49



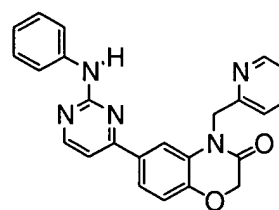
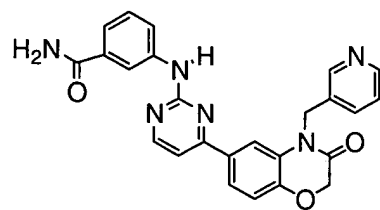
IVa-50



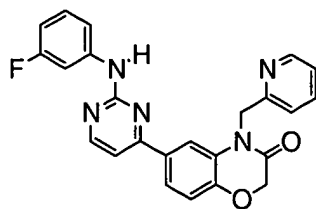
IVa-51



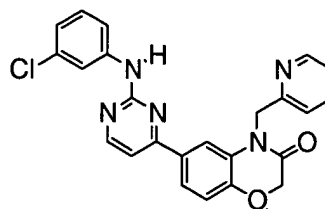
IVa-52



IVa-53

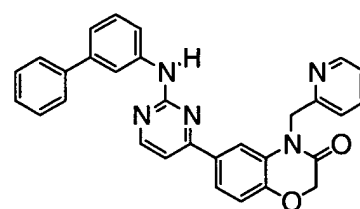
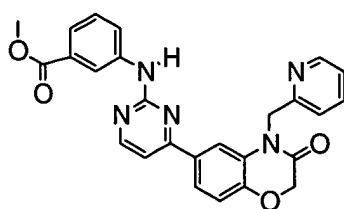
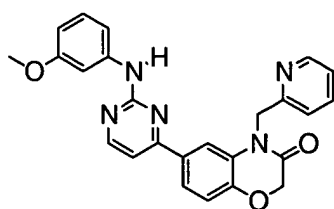


IVa-54



IVa-55

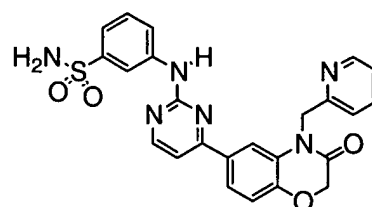
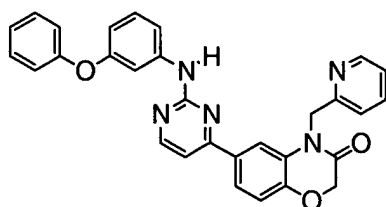
IVa-56



IVa-57

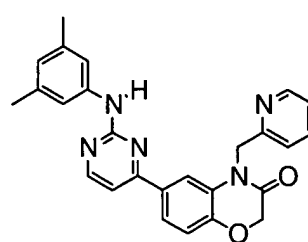
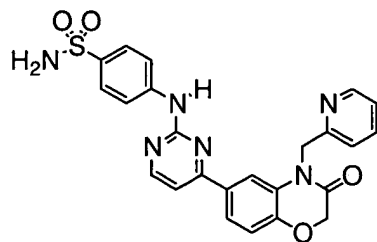
IVa-58

IVa-59



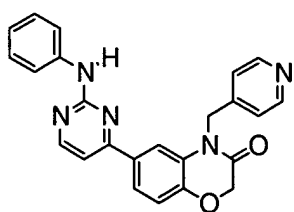
IVa-60

IVa-61

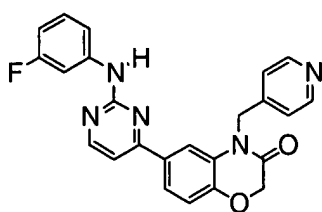


IVa-62

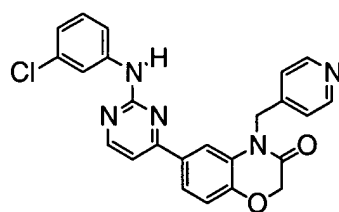
IVa-63



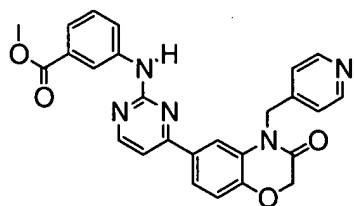
IVa-64



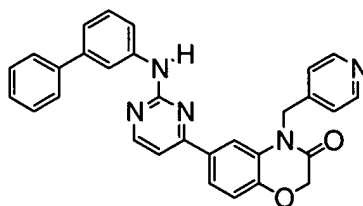
IVa-65



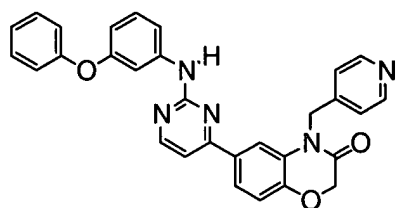
IVa-66



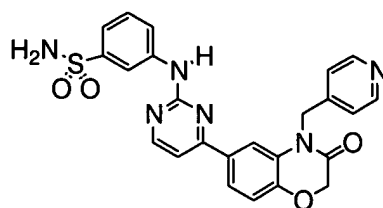
IVa-67



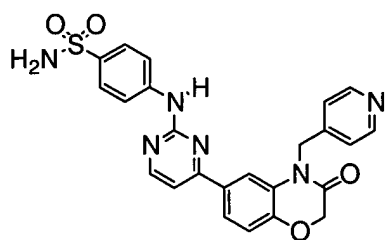
IVa-68



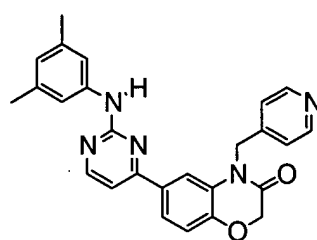
IVa-69



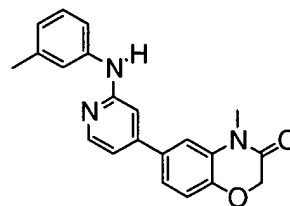
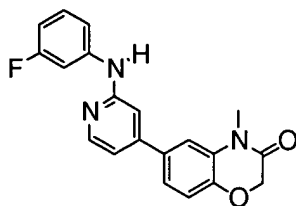
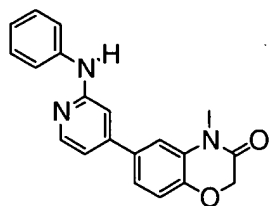
IVa-70



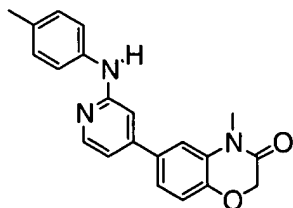
IVa-71



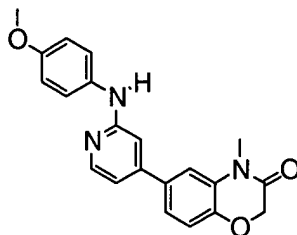
IVa-72



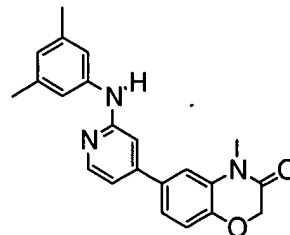
IVb-1



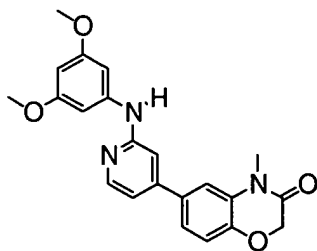
IVb-2



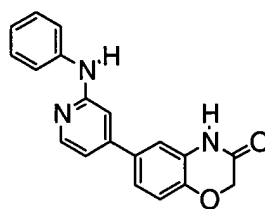
IVb-3



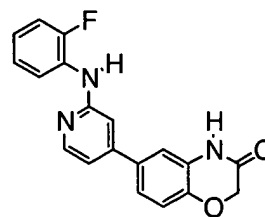
IVb-4



IVb-5



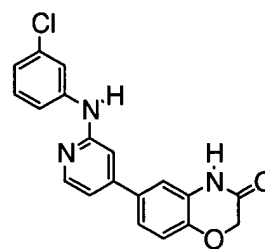
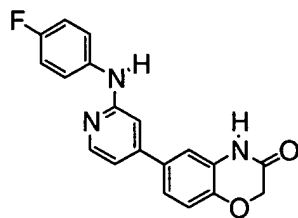
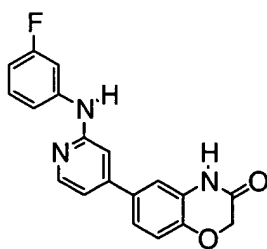
IVb-6



IVb-7

IVb-8

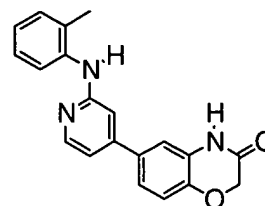
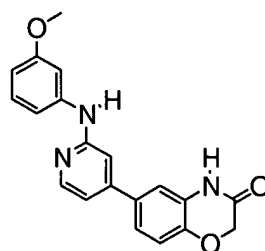
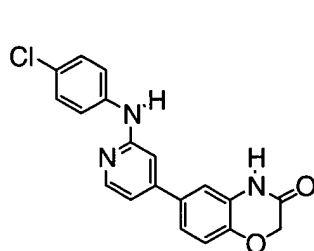
IVb-9



IVb-10

IVb-11

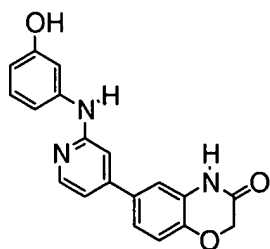
IVb-12



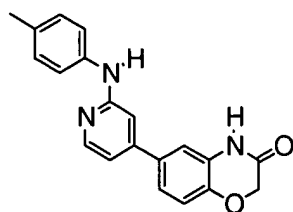
IVb-13

IVb-14

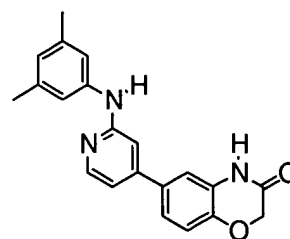
IVb-15



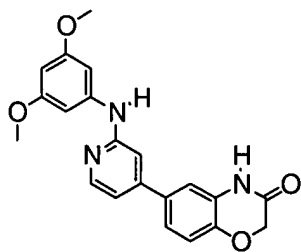
IVb-16



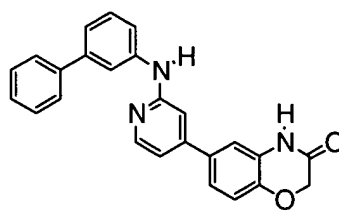
IVb-17



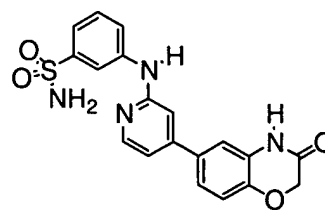
IVb-18



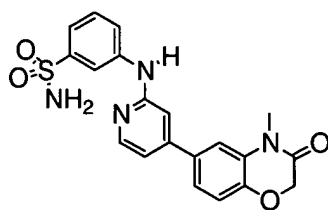
IVb-19



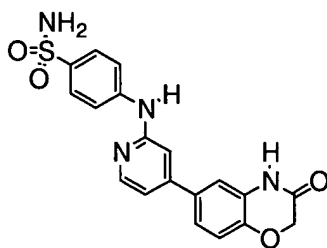
IVb-20



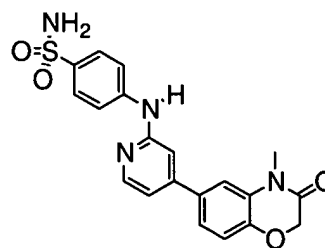
IVb-21



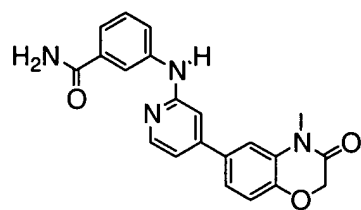
IVb-22



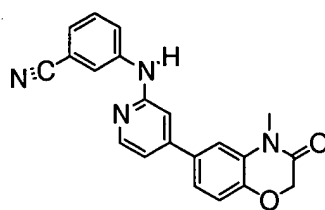
IVb-23



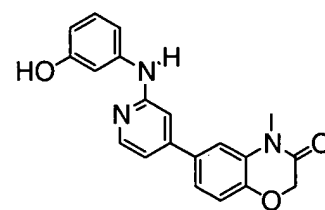
IVb-24



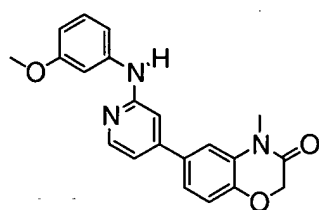
IVb-25



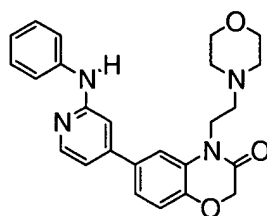
IVb-26



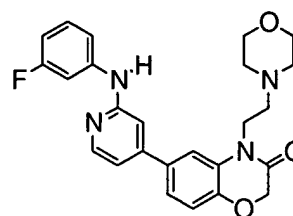
IVb-27



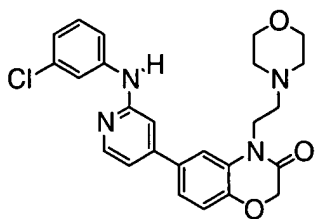
IVb-28



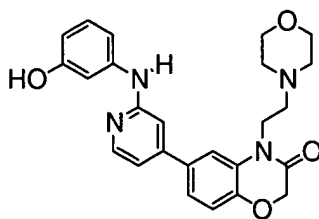
IVb-29



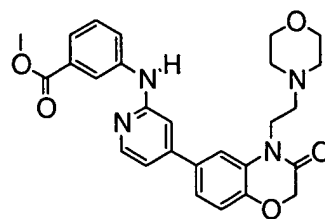
IVb-30



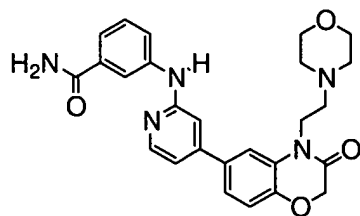
IVb-31



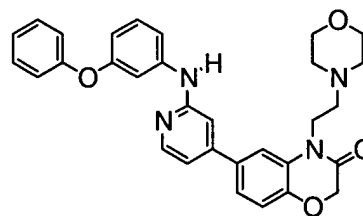
IVb-32



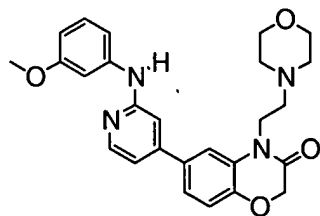
IVb-33



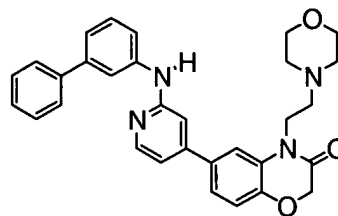
IVb-34



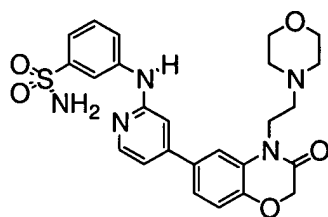
IVb-35



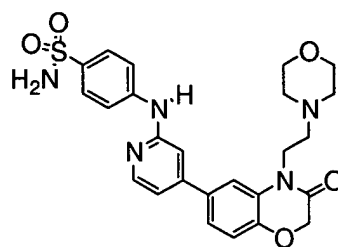
IVb-36



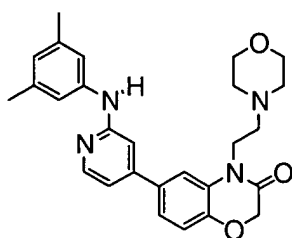
IVb-37



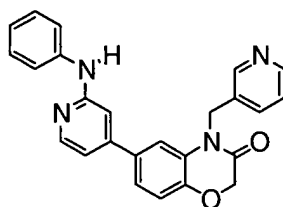
IVb-38



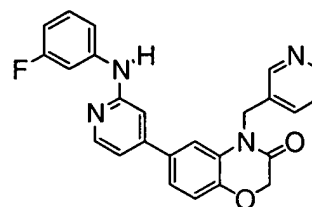
IVb-39



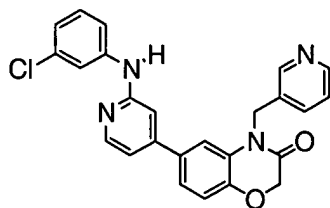
IVb-40



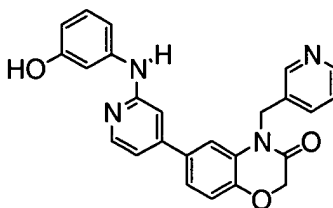
IVb-41



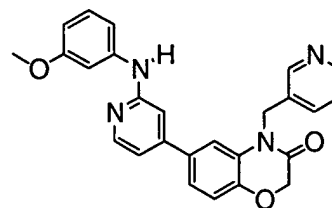
IVb-42



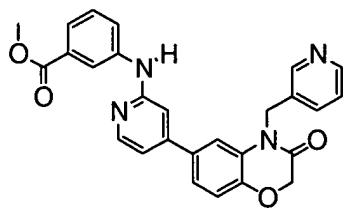
IVb-43



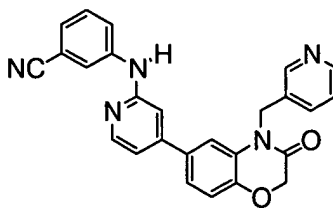
IVb-44



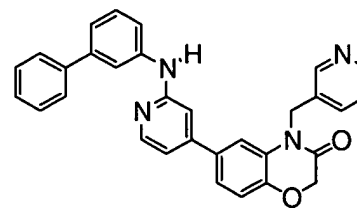
IVb-45



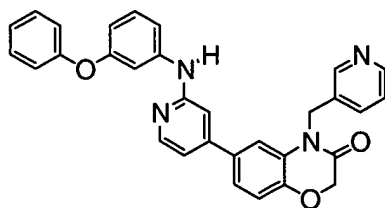
IVb-46



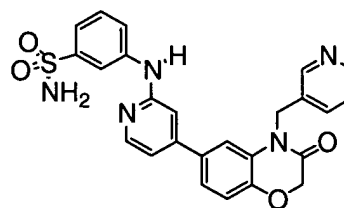
IVb-47



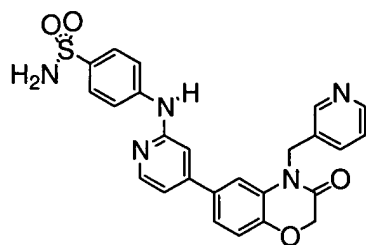
IVb-48



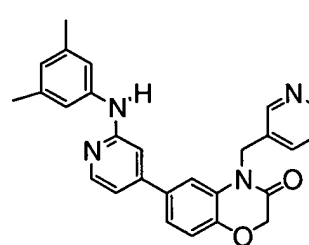
IVb-49



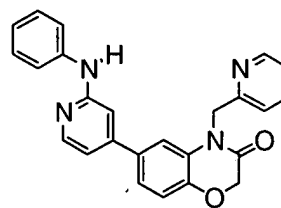
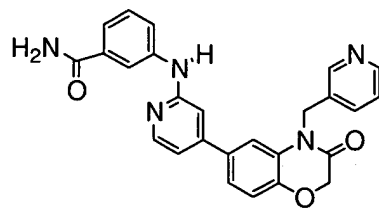
IVb-50



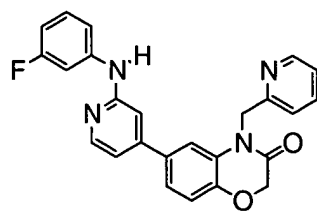
IVb-51



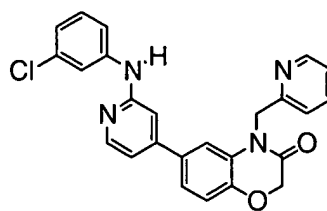
IVb-52



IVb-53

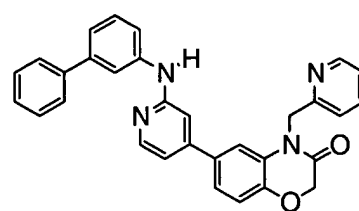
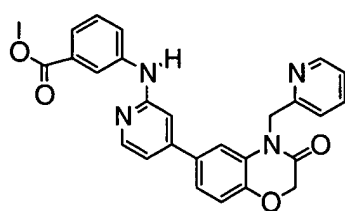
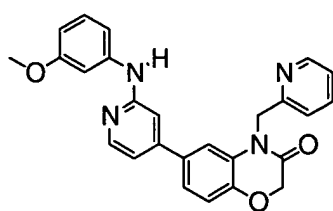


IVb-54



IVb-55

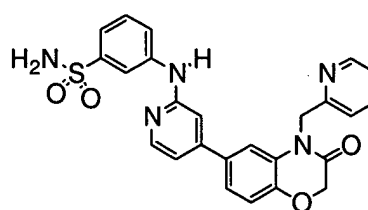
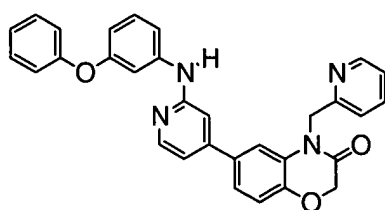
IVb-56



IVb-57

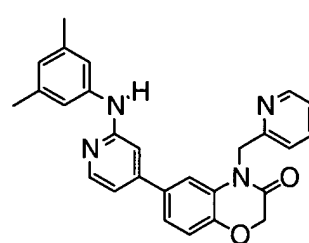
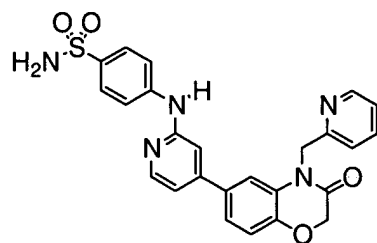
IVb-58

IVb-59



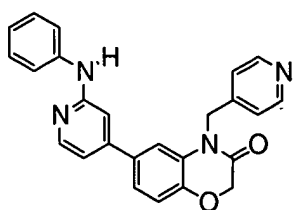
IVb-60

IVb-61

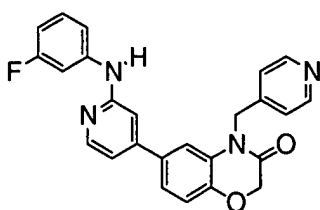


IVb-62

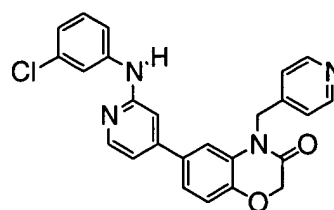
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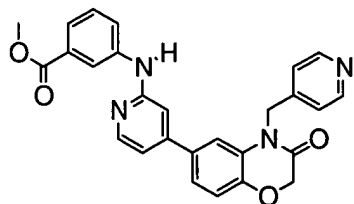
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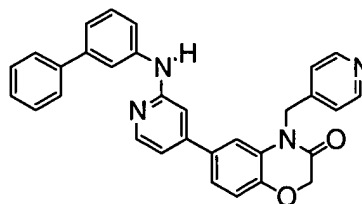
IVb-65



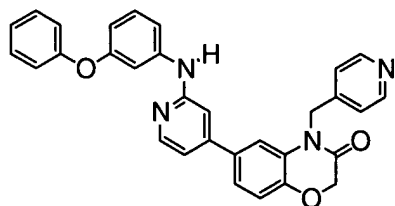
IVb-66



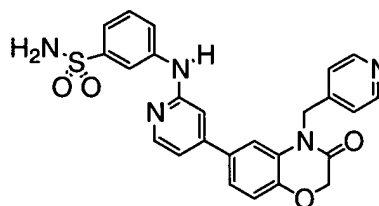
IVb-67



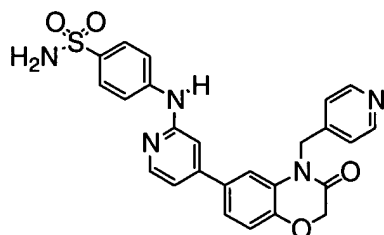
IVb-68



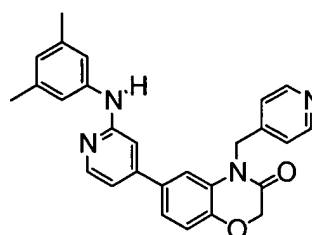
IVb-69



IVb-70



IVb-71



IVb-72.

or

24. A pharmaceutical composition comprising a compound according to claim 1, and a pharmaceutically acceptable carrier, adjuvant, or vehicle.

25. The composition of claim 24, further comprising an additional therapeutic agent selected from a chemotherapeutic or anti-proliferative agent, a treatment for Alzheimer's Disease, a

treatment for Parkinson's Disease, an agent for treating Multiple Sclerosis (MS), a treatment for asthma, an agent for treating schizophrenia, an anti-inflammatory agent, an immunomodulatory or immunosuppressive agent, a neurotrophic factor, an agent for treating cardiovascular disease, an agent for treating destructive bone disorders, an agent for treating liver disease, an agent for treating a blood disorder, or an agent for treating an immunodeficiency disorder.

26. A method of inhibiting JAK-3 kinase activity in:

- (a) a patient; or
- (b) a biological sample;

which method comprises administering to said patient, or contacting said biological sample with a compound of claim 1 or a composition of claim 24.

27. A method of treating or lessening the severity of a disease or disorder selected from an immune response, an autoimmune disease, a neurodegenerative, or a solid or hematologic malignancy comprising administering to a subject in need thereof a compound of claim 1 or a composition of claim 24.

28. The method of claim 27, wherein the disease or disorder is selected from an allergic or type I hypersensitivity reaction, asthma, transplant rejection, graft versus host disease, rheumatoid arthritis, amyotrophic lateral sclerosis, multiple sclerosis, Familial amyotrophic lateral sclerosis (FALS), leukemia, or lymphoma.

29. The method of claim 28, comprising the further step of administering to said patient an additional therapeutic agent selected from a chemotherapeutic or anti-proliferative agent, a treatment for Alzheimer's Disease, a treatment for Parkinson's Disease, an agent for treating Multiple Sclerosis (MS), a treatment for asthma, an agent for treating schizophrenia, an anti-inflammatory agent, an immunomodulatory or immunosuppressive agent, a neurotrophic factor, an agent for treating cardiovascular disease, an agent for treating destructive bone disorders, an

agent for treating liver disease, an agent for treating a blood disorder, or an agent for treating an immunodeficiency disorder, wherein:

said additional therapeutic agent is appropriate for the disease being treated; and

said additional therapeutic agent is administered together with said composition as a single dosage form or separately from said composition as part of a multiple dosage form.